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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/660,878

09/12/2003

Karnail S. Atwal

HA726 DIV

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04/25/2005

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EXAMINER

RAO, DEEPAK R

ART UNIT

PAPER NUMBER

1624

DATE MAILED: 04/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.		Applicant(s)	
	10/660,878		ATWAL ET AL.	
	Examiner		Art Unit	
	Deepak Rao		1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 January 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 61-85 ~~is~~ are pending in the application.
- 4a) Of the above claim(s) 64, 65 and 80 ~~is~~ are withdrawn from consideration.
- 5) ☒ Claim(s) 78 is/are allowed.
- 6) ☒ Claim(s) 61-63, 66-77, 79 and 81-85 ~~is~~ are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>121604 & 040405</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

This office action is in response to the amendment filed on January 31, 2005.

Claims 61-85 are pending in this application.

Election/Restrictions

Claims 64, 65 and 80 are withdrawn from further consideration by the examiner pursuant to 37 CFR 1.142(b), as being drawn to a non-elected species. The non elected species and the generic subject matter drawn to the non elected species from claims 61-63, 66-79 and 81-83 are also withdrawn from further consideration.

Withdrawn Rejections/Objections:

Applicant is notified that any outstanding rejection/objection that is not expressly maintained in this office action has been withdrawn or rendered moot in view of applicant's amendments and/or remarks.

The following rejections are maintained:

1. Claims 69-77 and 79 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of atrial arrhythmias, does not reasonably provide enablement for the treatment of all other diseases of the instant claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The reasons provided in the previous office action are incorporated here by reference.

Art Unit: 1624

Applicant's arguments and the cited references have been fully considered but they were not deemed to be persuasive. Applicant has not provided any evidence to show that the instantly claimed compounds are effective in treating all types of disorders falling within the scope of instant claims. Applicant cited several references having publication dates ranging from 1999-2004. However, evidence that the compounds are effective in the treatment of claimed disorders must have been available as of the filing date in order to provide an enabling disclosure. Accordingly, the references having a publication date prior to the filing of the instant application are considered as state of the art.

Koh et al., cited by applicant provides 'potassium channels control contraction of gastrointestinal smooth muscles', however, the reference does not provide a method of treating all types of gastrointestinal disorders by administering compounds having potassium channel inhibitory activity. In fact it is submitted in the reference - "Transgenic knock-out animals would provide conclusive evidence for this assignment". The scope of the instant claims includes all types of gastrointestinal disorders such as inflammatory bowel diseases, e.g., ulcerative colitis, Crohn's disease, etc. as per the disclosure in the specification. The therapeutic method of the instant claims includes treatment of Crohn's disease and ulcerative colitis, which have been proven very difficult to treat because 'there is no known cause' (see The Merck Manual). Bremner et al. (Expert Opin. Pharmacother. 2002) provide that "New therapies that affect immunomodulation offer the possibility of disease control in those unresponsive to conventional therapy and may reduce the need for further surgery. However, these treatments remain to be fully evaluated" (see page 820). Singh et al. (British Journal of Surgery, 2001) provide that 'the etiology and pathogenesis of inflammatory bowel diseases are incompletely

Art Unit: 1624

understood' (see page 1558). Robinson (Eur. J. Surg. 1998) indicates that "Despite the growing list of medications and formulations prompted for the treatment of IBD, no single drug or recognized combination has yet been confirmed as dependably clinically effective"; "All physicians who care for UC and CD patients enthusiastically await more optimal regimens for these challenging disorders" (see page 90). This is indicative of the unpredictability related to the treatment of gastrointestinal disorders and the cited references do not provide any evidence to the contrary.

The scope of the instant claims includes the treatment of cognitive disorders and applicant has not provided any state of the art reference which provides sufficient evidence for the instant claims. Rho et al. (Dev Neurosci 1999), provide that 'potassium channels play a critical role in neuronal excitability' and therefore, the activity may be linked to epilepsy. Cochran et al. (Eur J Neurosci 2001) also provide that 'a blocker of voltage-activated K^+ channels produce seizure activity', however, the reference does not provide nexus between the potassium channel inhibitory activity and treatment of cognitive disorders generally.

The scope of instant claims also includes 'treatment of diabetes' and applicant provides some references as state of the art, however, these were all published after the filing date of the instant application and not available at the time of filing. One of the cited reference MacDonald et al. (Diabetologia 2003) indicates that 'further studies characterizing tissue specific differences in Kv2.1 currents and the roles and regulation of the various Kv channels expressed in insulin-secreting cells may provide agents with sufficient beta-cell specificity to be considered for therapeutic use'. This is indicative of the experimentation involved for the therapeutic agent to

Art Unit: 1624

be used in treatment of the disorder. For all the above reasons, the rejection is hereby maintained.

2. Claims 61-63, 66-69 and newly added claim 84 are rejected under 35 U.S.C. 102(b) as being anticipated by Tsuda et al., EP 217,142. The reasons provided in the previous office action are incorporated here by reference.

Applicant's arguments have been fully considered but they were not deemed to be persuasive. Applicant relies on the proviso statement in the definition of R^{3*} to overcome the rejection, however, the claims continue to read on the exemplified compound of the reference, see e.g., compound no. 99, wherein the substituent analogous to R^{3*} of the instant claim is $-\text{CO}-\text{NH}-\text{CH}(\text{CH}_3)_2$, which falls within the genus of the instant claim. The instant claim recites that Z^{5*} is substituted alkyl, however, does not provide what substituents are included. The group $-\text{CH}(\text{CH}_3)_2$ may also be considered as a substituted alkyl group. Also, see the compound No. 156 in the reference (page 46), which is excluded from claim 61 (see the proviso that Z^{5*} and Z^{6*} together do not form unsubstituted piperidiny), however, the newly presented claim 84 includes such compound.

3. Claims 61-63, 66-69 and 81-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsuda et al., EP 217,142, in view of applicant's submission. The reasons provided in the previous office action are incorporated here by reference.

Applicant argues that the instantly claimed compounds do not fall within the scope of the reference. However, as indicated above, the instant claims read on reference compounds and the

Art Unit: 1624

specific compounds recited in the remaining claims are structural analogs that fall within the genus taught in the reference. The reasons provided under 35 U.S.C. 102 rejection above are incorporated here.

4. Claims 61-63, 66-69, 81-83 and 85 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 6,706,720. The reasons provided in the previous office action are incorporated here by reference.

Applicant's arguments have been fully considered but they were not found to be persuasive. The compounds issued in US'720 are encompassed by the instant claims and therefore, the instant claims are not patentably distinct. The definition of R^{3*} in the instant claims includes heterocyclo and $-\text{CONZ}^{5*}\text{Z}^{6*}$ wherein Z^{5*} and Z^{6*} together with the nitrogen atom form a heterocyclic group. The reference compounds are drawn to the same core having a benzimidazole or substituted pyrrolidin-1-yl group, see claim 1. Applicant further argues that the rejection is improper because the instant divisional application resulted based on a restriction requirement in the parent application. However, when the prosecution history of the parent application was reviewed, it was noted that the entire class of pyrazolo[1,5-a]pyrimidine compounds were grouped together and search and examination was based on the elected species. During prosecution, applicant filed a narrower subgenus which was found to be allowable. Since the instantly claimed genus overlaps the reference genus, the rejection is proper.

Art Unit: 1624

The following rejections are necessitated by the amendment:

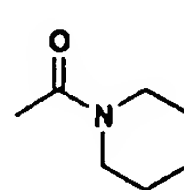
Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

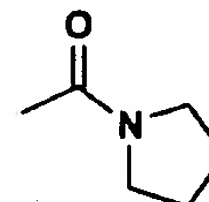
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 84 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 84 recites the limitation "R^{3*} is selected from



or



" in

lines 2-3. There is insufficient antecedent basis for this limitation in claim 61 on which claim 84 is dependent. Claim 61 excludes these substituent groups, see the proviso statement in the definition of Z^{5*} and Z^{6*} (provided below for convenience):

or Z^{5*} and Z^{6*} may together with the nitrogen atom to which they are bonded form a heterocyclic group or substituted heterocyclic group, provided that Z^{5*} and Z^{6*} do not together form unsubstituted piperidinyl, unsubstituted pyrrolidinyl, or unsubstituted morpholinyl;

Allowable Subject Matter

Claim 78 is allowed. The references of record do not teach or fairly suggest the use of the claimed compounds for treating epilepsy. Applicant provided evidence that potassium channel activity is linked to the therapeutic method of treating epilepsy.

Art Unit: 1624

Receipt is acknowledged of the Information Disclosure Statements filed on December 16, 2004 and April 4, 2005 and copies are enclosed herewith.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund Shah, can be reached on (571) 262-0674. If you are unable to reach Dr. Shah within a 24 hour period, please contact James O. Wilson, Acting-SPE of 1624 at (571) 272-

Art Unit: 1624

0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Deepak Rao
Primary Examiner
Art Unit 1624

April 18, 2005